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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/599,292

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Adam Liebert

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EXAMINER

GUPTA, VANI

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/599,292	Applicant(s) LIEBERT ET AL.	
	Examiner VANI GUPTA	Art Unit 3768	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 February 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 and 17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 24, 2010 has been entered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. ***Claims 1, 3, 4, 7, 8, 11, 13, 14, 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Sevick-Muraca et al. (US 7,328,059 B2).***

Regarding Claim 1, Sevick-Muraca et al. (hereinafter *Sevick*) describes a method for detecting a dye bolus injected into the body of a living being, comprising the steps of:

- a. injecting a non-specific (non-binding) fluorescent contrast agent within a short amount of time (or introducing a “dye bolus”) into the body (*col. 3, ll. 1 – 28; col. 7, ll. 6 – 9*);

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b. irradiating an optical excitation radiation into a predetermined region of the body, the excitation radiation being chosen so as to excite a fluorescence radiation of the non-specific fluorescent dye (*col. 6, ll. 22 – 25; col. 7, ll. 16 – 17*); and

c. detecting the fluorescence radiation occurring on the surface of the body (*“image of tissue,” col. 3, ll. 17 – 21*),

and wherein the flight time is determined during the transit of the dye bolus (“uptake”) through the tissue so as to obtain a profile of the photon flight time over the transit (“spatial differences,” “uptake”) time of the dye bolus (*col. 7, line 26 – col. 8, line 64; col. 13, ll. 45 – 67; col. 15, line 15 – col. 16, line 39; col. 20, ll. 60 – 67; col. 23, ll. 23 – 49*), the profile being used to evaluate the tissue (*col. 7, ll. 40 – 43*).

Regarding Claim 3, Sevick suggests that time course of the fluorescence radiation is determined with nanosecond time resolution (*col. 14, ll. 35 – 37*).

Regarding Claim 4, Sevick suggests blocking off the frequency of the excitation radiation by filtering for the detection of the fluorescence radiation (*col. 6, ll. 26 – 29*).

Regarding Claim 7, Sevick suggests evaluating detecting fluorescence radiation by assessing the distribution of the measured time of flight photons (see last part of rejection of Claim 1).

Regarding Claim 8, Sevick discusses monitoring and mapping fluorescence characteristics using time-based measurements, including the start of dye bolus detection. This start is represented by the darkening of image regions due to the fluorescing dye that is absorbing radiation. One of the time-based measurements used is “mean ‘time-of-flight’,” or “the mean

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time between the absorption of an excitation photon and emission of a fluorescent photon” (*col. 13, line 62 – col. 14, line 22*).

Regarding Claim 11, Sevick discloses a device for detecting a fluorescent dye bolus injected into the body of a living being (**fig. 1, 110**; *col. 6, ll. 5 – 67*), comprising:

- a. an optical radiation source (“*modulated light source*,” **120**) for irradiating an excitation radiation into the body, said excitation radiation being chosen so as to excite a fluorescence radiation of the fluorescent dye (*col. 6, ll. 11 – 21*);
- b. a detection arrangement (“*detection subsystem*,” **140**) for detecting a fluorescence radiation of the fluorescent dye (*col. 6, ll. 22 – 51*); and
- c. a measurement device (“*processor*,” **160**) for detecting a time difference between a time of irradiation of said excitation and a time of detection of said fluorescence radiation (*col. 6, line 52 – col. 7, line 53*).

Regarding Claim 13, Sevick explains that the detection arrangement disclosed above is designed to detect the time course of fluorescence radiation with nanosecond or picosecond time resolution (*col. 14, ll. 23 – 37*).

Regarding Claim 14, Sevick explains that the detection arrangement disclosed above comprises an optical filter for blocking off the radiation, or for “obtaining a *selected* emission wavelength corresponding to emission of designated fluorophore in tissue” (*col. 6, ll. 26 – 29*).

Regarding Claim 17, Sevick discloses a method for detecting a dye bolus within the body of living being, comprising the steps of;

- a. injecting a fluorescent dye bolus into the body (*col. 7, ll. 6 – 7*);

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- b. irradiating an optical excitation radiation into a predetermined region of the body, the excitation radiation being chosen so as to excite a fluorescence radiation of the fluorescent dye (*col. 7, ll. 16 – 17*);
- c. detecting the fluorescence radiation on the surface of the body, wherein a high frequency modulated light is used as the excitation radiation and the modulation depth and the phase of the fluorescence radiation are determined (*col. 7, ll. 8 – 15*) in order to determine the flight time of fluorescence photons, and wherein the flight time is determined during the transit of the dye bolus through the tissue so as to obtain a profile of the photon flight time over the transit time of the dye bolus, the profile being used to evaluate the tissue (*please see rejection of claim 1*).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Inventorship

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. *Claims 2 and 12 are rejected under 35 USC 103(a) as being unpatentable over Sevick-Muraca et al. (US 7,328,059 B2) as applied to Claim 1 above, in view of Kessler et al. (US 5,610,932).*

Regarding claims 2 and 12, Sevick suggests method and apparatus for detecting a (fluorescent) dye bolus injected into the body of a living being, as explained above.

However, Sevick does not suggest specifically emitting an excitation radiation from an optical radiation source a short pulse with a pulse width in the picosecond range.

Nonetheless, *Kessler et al.* (hereinafter *Kessler*) teaches that it is known in the art to emit a excitation radiation pulse with a pulse width in the picosecond range for fluorescence detection (*col. 1, ll. 5 – 19*).

It would be prima facie obvious to modify Sevick with Kessler to so that one could detect fluorescence with greater flexibility, as explained by Kessler.

3. *Claim 9 is rejected under 35 USC 103(a) as being unpatentable over Sevick-Muraca et al. (US 7,328,059 B2) as applied to Claim 1 above, in view of Boas (US 6,516,214).*

Regarding Claim 9, Sevick suggests method and apparatus for detecting a (fluorescent) dye bolus injected into the body of a living being, as explained above.

However, Sevick does not suggest specifically that the region irradiated by sid xcitation radiation is at the head in order to examine the brain.

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Nonetheless, *Boas* teaches administering a dye bolus into the blood stream of a patient, directing light into the brain of the subject, and detecting light emitted from the brain over time at a detection location (*col. 2, ll. 4 – 26*).

It would be prima facie obvious to modify *Sevick* with *Boas* so that one could also use the detection of high and low oxygenation levels by determining decrease or increases in intensity of scattered light for diseased tissue diagnosis (*Boas: col. 1, ll. 45 – 50*).

4. *Claim 10 is rejected under 35 USC 103(a) as being unpatentable over Sevick-Muraca et al. (US 7,328,059 B2) as applied to Claim 1 above, in view of Zhao et al. (US 2003/0031628 A1).*

Regarding Claim 10, *Sevick* suggests method and apparatus for detecting a (fluorescent) dye bolus injected into the body of a living being, as explained above.

However, *Sevick* does not suggest specifically emitting an excitation radiation from an optical radiation source in the area of the lungs.

Nonetheless, *Zhao et al.* describes an experimentation involving first injecting mice suffering from tumors with dye bolus, and then directing optical excitation radiation into the area of the lungs. The tumor areas fluoresced as a result of the application of excitation radiation (*para. [0045]*).

It would be prima facie obvious to modify *Sevick* with *Zhao et al.* so that one could also make use of fluorescent optical tumor imaging (FOTI), which permits real-time observation and monitoring of progression of infection on a continuous basis (*Zhao et al.: para. [0045]*).

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5. Claims 5, 6, and 15 are rejected under 35 USC 103(a) as being unpatentable over Sevick-Muraca et al. (US 7,328,059 B2) as applied to Claim 1 above, in view of Folestad et al. (US 6,794,670 B1).

Regarding claims 5, 6, and 15, Sevick suggests method and apparatus for detecting a (fluorescent) dye bolus injected into the body of a living being, as explained above.

However, Sevick does not suggest specifically detecting the excitation radiation diffusely reflected from the body simultaneously and in parallel to detecting the fluorescence radiation from the tissue; and accomplishing this in a time-resolved manner.

Nonetheless, *Folestad et al.* discusses detecting the radiation reflected from the sample as well as the diffusely backscattered radiation by a single lens (*fig. 1b, L4'*); and accomplishing it in a time-resolved manner (*col. 6, ll. 35 – 54*).

It would be prima facie obvious to modify Sevick with Folestad et al. so that one could accomplish both tasks in time-resolved manner using one component of the same apparatus, which would take up less resources (cost, infrastructure, material, etc.)

Response to Arguments

Applicant's arguments with respect to the rejections of claims 1, 3, 4, 7, 8, 11, 12, 14, and 17 as applied to Sevick have been fully considered but are not persuasive. Applicant argues that Sevick does not suggest measuring profile of time of flight over transit time of the dye bolus. More specifically, Applicant argues that Sevick does not “monitor the movement of the dye bolus,” or “form a profile of the time of flight measurements during the time when the dye bolus transits,” but rather obtains a “snapshot of the pattern of the stationary distribution of fluorescence.”

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Examiner respectfully disagrees. First of all, Examiner respectfully points out that the claim language does not actually suggest a step of monitoring the movement of the dye bolus. As currently written, this portion of claim suggest obtaining or deriving photon flight time as a function of a time it takes for the dye bolus to move from one position to the next. As discussed above, flight time is determined during the transit of the dye bolus (“uptake”) through the tissue so as to obtain a profile of the photon flight time over the transit (“spatial differences,”) time of the dye bolus (*col. 7, line 26 – col. 8, line 64; col. 13, ll. 45 – 67; col. 15, line 15 – col. 16, line 39; col. 20, ll. 60 -67; col. 23, ll. 23 – 49*), the profile being used to evaluate the tissue (*col. 7, ll. 40 – 43*). In any case, as indicated in these passages, Sevick is monitoring movement of the dye, as in “uptake” of the fluorophores into tissue, affecting concentration of tissue, thereby helping determine condition of tissue.

Applicant’s arguments, with respect to the rejection(s) of claim(s) 2 and 12 under Ntziachristos have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Kessler, as indicated above.

Applicant's arguments with respect to claims 5, 6, 9, 10, 15, have been considered but are moot in light of above responses.

Conclusion and Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANI GUPTA whose telephone number is (571)270-5042. The examiner can normally be reached on Monday - Thursday (8:30 am - 6:00 pm; EST).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/V. G./
Examiner, Art Unit 3768

/Long V Le/
Supervisory Patent Examiner, Art Unit 3768